

### REMARKS

Applicants observe that the Office Action mailed May 30, 2003 was mailed to Lahive & Cockfield. Applicants respectfully point out that a Change of Attorney Docket Number and Change of Correspondence Address were submitted to the USPTO on December 17, 2002. Applicants respectfully request that the Examiner use the current correspondence address and docket number on file.

Reconsideration of the Office Action mailed May 30, 2003, (hereinafter "instant Office Action"), and withdrawal of the rejection claims 1-138, are respectfully requested.

In the instant Office Action, claims 1-138 are listed as pending and claims 1-138 are listed as rejected.

The Examiner has noted that no prior art has been identified as to the elected species (Example 207 on page 299), thus the search has been extended to the entire genus.

The Examiner comments at page 2 of the Office Action regarding the proper content of an Abstract. Applicants have amended the Abstract to follow the guidelines pointed out by the Examiner. The replacement of the pending Abstract with the replacement Abstract is effected by the amendment hereinabove.

The Examiner has rejected Claim 120 under 35 U.S.C. §112, first paragraph, for allegedly not reasonably providing enablement for an ocular condition, cancer, chronic inflammation, cardiovascular condition and stroke. Applicants respectfully traverse this rejection. Without conceding the correctness of the Examiner's rejections and for the sole purpose of advancing the prosecution of the instant application to place it in condition for allowance, Applicants have canceled ocular condition, cancer, chronic inflammation, cardiovascular condition and stroke from claim 120, without waiver or prejudice to Applicants' right to file a continuation application to the cancelled subject matter. Applicants have also cancelled claims 121, 122 and 123 and incorporated the subject matter of claims 121, 122 and 123 into claim 120. Accordingly, the rejection of claim 120 under 35 U.S.C. §112, first paragraph, is obviated and should be withdrawn.

The Examiner has rejected Claim 115 under 35 U.S.C. §112, first paragraph, for allegedly containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make

and/or use the invention. The Examiner alleged that the specification does not teach the method of affecting hyperproliferative disorders. Applicants respectfully traverse this rejection. Without conceding the correctness of the foregoing rejection and for the sole purpose of advancing the prosecution of the instant application to place it in condition for allowance, Applicants have canceled claim 115, without waiver or prejudice to Applicants' right to file a continuation application to the canceled subject matter. Accordingly, the rejection of claim 115 under 35 U.S.C. §112, first paragraph, is obviated and should be withdrawn.

The Examiner has rejected Claim 1-138 under 35 U.S.C. §112, second paragraph, for the reasons set out at pages 12 to 14 of the instant Office Action. The following are Applicants' responses referenced according to the paragraphs in the Office Action pertaining to this rejection.

a. The Examiner has rejected Claim 1 and claims dependent thereon because the term "prodrug" is allegedly indefinite. Applicants respectfully traverse this rejection. The inclusion of "prodrugs" in a claim is analogous to including the phrase "pharmaceutically acceptable salts thereof" in that the metes and bounds of a prodrug are as clear and definite to one skilled in the art as the metes and bounds of the term "pharmaceutically acceptable salts thereof". It is clearly understood that a pharmaceutically acceptable salt of a claimed compound may be used in place of the claimed compound. With respect to the inclusion of "prodrugs" in a compound claim, the meaning of the term is equally clear in that "prodrug" refers to a compound that is converted to an active drug by a metabolic biotransformation, see Chapter 8, entitled "Prodrugs and Drug Delivery Systems," in *The Organic Chemistry of Drug Design and Drug Action*, by Richard Silverman, © 1992 Academic Press, San Diego (hereinafter "Silverman"), a copy of which is enclosed herewith for the Examiner's convenience as Exhibit A.

Silverman provides clear evidence that one of ordinary skill in the art is aware of the prodrugs that are commonly used in the art. Further, Silverman teaches how to make prodrugs generally. In addition, it is well known in the art of pharmaceutical chemistry how to make prodrugs. The chemistry of prodrugs is such that it is generally applicable and depends on the presence of functional groups and not the structure of the core compound. Accordingly, this rejection under 35 U.S.C. §112, second paragraph, is overcome and should be withdrawn.

b. The Examiner alleges that the moiety "(C<sub>1</sub>-C<sub>6</sub>)" in, *inter alia*, claim 1 is unclear because it is not clear to the Examiner whether Applicants intend it to be an alkyl group or

otherwise. Applicants direct the Examiner's attention to page 66, lines 3-5, of the specification which defines such a moiety as "(C<sub>0</sub>-C<sub>6</sub>)" as referring to a straight chain, branched or cyclic aliphatic group that is completely saturated or having one or more units of unsaturation. Therefore, Applicants submit that the moiety "(C<sub>1</sub>-C<sub>6</sub>)" is not indefinite and is clear and definite according to the definition in the specification. Accordingly, this rejection under 35 U.S.C. §112, second paragraph, is obviated and should be withdrawn.

c. The Examiner alleges that the phrase "an optionally substituted (C<sub>1</sub>-C<sub>6</sub>)" is incorrect in the definition of Z<sup>111</sup> since Z<sup>111</sup> is divalent and, thus, should read "an optionally substituted (C<sub>1</sub>-C<sub>6</sub>)alkylene". Applicants point out that for the same reason as given in Applicants' response in paragraph b immediately hereinabove, the phrase as Applicants have it for the definition of Z<sup>111</sup>, that is "an optionally substituted (C<sub>1</sub>-C<sub>6</sub>)", is correct. For example, the phrase as it currently reads is intended to cover not only "alkylene" but also "alkenylene" and "alkynylene", among others as encompassed by the definition given at page 66, lines 3-5 of the instant specification. Accordingly, this rejection under 35 U.S.C. §112, second paragraph, is obviated and should be withdrawn.

d. The Examiner alleges that the term "amido" is indefinite as used in claim 1, page 927, line 19 and elsewhere in the claims. Applicants respectfully traverse this rejection. The term "amido" is intended to represent a radical amide group, i.e. -C(O)NH<sub>2</sub>. As the Examiner will note, it is the carbon end that is to be bound to G or Z<sup>100</sup> and it is the amine portion of the amide group that can be substituted or unsubstituted. With respect to what the substituent(s) can be on the amine, Applicants direct the Examiner's attention to page 67, lines 1 -14 of the specification, which describes the types of substituents that can be attached to the amino nitrogen. The definition is definite and clear as to the subject matter that is encompassed by the phrase "substituted amido". Accordingly, this rejection under 35 U.S.C. §112, second paragraph, is obviated and should be withdrawn.

e. The Examiner has pointed out that the term "comprising" is used in claim 1, page 930, line 11, and suggests replacing it with "consisting of". Applicants have amended claim 1 as suggested by the Examiner. Accordingly, this rejection under 35 U.S.C. §112, second paragraph, is obviated and should be withdrawn.

f. The Examiner alleges that the term “azacycloalkyl” is indefinite. Applicants note that the prefix “aza” indicate that there are at least two nitrogens in that ring. The rest of the ring are indeed carbon atoms, otherwise another name element would be included, e.g., if it included a sulfur atom it would have been named as azathiocycloalkyl. Therefore, other heteroatoms are not intended to be included by the term “azacycloalkyl”. Accordingly, this rejection under 35 U.S.C. §112, second paragraph, is obviated and should be withdrawn.

g. The Examiner alleges that the phrase “biologically active metabolites” in claim 1 is not clear. Without conceding the correctness of the foregoing rejection and for the sole purpose of advancing the prosecution of the instant application to place it in condition for allowance, Applicants have amended claim 1 to delete the phrase “biologically active metabolites”. Applicants have also amended claims 38, 45, 48, 89, 101, 107-113, 116, 118, 120 and 125 to delete the phrase “biologically active metabolites”. Accordingly, the rejection of claim 1 under 35 U.S.C. §112, second paragraph, is obviated and should be withdrawn.

h. The Examiner alleges that in claim 113, the phrase “one or more protein kinase” is indefinite. Applicants respectfully traverse this rejection. Applicants have clearly taught how to test a compound of the present inventions’ ability to inhibit a protein kinase at, *inter alia*, pages 99 to 108. Although the assays are illustrated using certain protein kinases, the assays are generally applicable to other protein kinases. Therefore, one of ordinary skill in the art can test Applicants’ compound’s ability to inhibit any number of protein kinases using routine experimentation. Having determined which protein kinases are inhibited by a compound, one would know which protein kinases are inhibited upon administration of a compound according to the method of claim 11. Accordingly, claim 11 is not indefinite and the rejection of claim 11 under 35 U.S.C. §112, second paragraph, should be withdrawn.

i. The Examiner has rejected claim 126 because it allegedly fails to further limit claim 116. Applicants respectfully traverse this rejection. However, without conceding the correctness of the foregoing rejection and for the sole purpose of advancing the prosecution of the instant application to place it in condition for allowance, Applicants have canceled claim 126, without waiver or prejudice to Applicants’ right to file a continuation application to the canceled subject matter. Accordingly, the rejection of claim 126 under 35 U.S.C. §112, second paragraph, is obviated and should be withdrawn.

Claims 49, 95 and 129 have been amended to correct typographical errors. Claims 128 and 130, which previously depended from claim 126, which has been cancelled, have been amended to depend from claim 116.

No fees are due for the instant amendment since the total number of claims after entry of the amendments hereinabove is not more than the total number of claims that Applicants have paid for to date.

Based upon the foregoing, Applicants believe that claims 1-138 are in condition for allowance. Prompt and favorable action is earnestly solicited.

If the Examiner believes that there are any issues that could be resolved in a telephone conference, Applicants invite the Examiner to call Applicants' undersigned agent.

Respectfully submitted,

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